IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Graham Sommer	Attorney Docket No.: STFUP145/S03-109
Application No.: 10/693,068	Examiner: Lamprecht, Joel
Filed: October 23, 2003	Group: 3737
Title: MEASUREMENT OF RENAL EXTRACTION FRACTION USING CONTRAST ENHANCED COMPUTED TOMOGRAPHY	Confirmation No.: 2220

DECLARATION OF GRAHAM SOMMER UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Graham Sommer, hereby declare the following:

1. I am the sole inventor for all matters within the above captioned patent application.

2. The above captioned patent application is presently assigned to The Board of Trustees of the Leland Stanford Junior University of Palo Alto, California.

3. I am presently a Professor of Radiology at Stanford University, School of Medicine.

4. I have more than 30 years of experience practicing as a clinical research physician at Stanford in the field of diagnostic radiology, with a particular emphasis on advanced imaging techniques using computed tomography, magnetic resonance imaging and ultrasound imaging to characterize tissues.

5. I am familiar with the teachings of U.S. Patent 6,122,540 by Katzberg and U.S. Patent 6,071,494 by Unger cited in the Office Action dated October 16, 2009 and with the field of medical diagnostic imaging of renal functions.

6. In my opinion, Katzberg teaches a magnetic resonance imaging (MRI) method for measuring renal hemodynamic functions using Gadolinium DTPA (Gd-DTPA) as a paramagnetic contrast agent (Katzberg Col. 2:26-32). A time series of MRI images are captured at a particular spatial location and orientation, and a longitudinal relaxation T_1 value is estimated by measuring a rate of change in image density in the time series of images at the particular location captured. Both an arterial T_1 (T_1A) and a venous T_1 (T_1V) are estimated using the time image series (Katzberg Col. 3:49-67, Figure). For MRI imaging, the longitudinal relaxation T1 value is related non-linearly to a concentration of the paramagnetic contrast agent Gd-DTPA as expressed by Equation (3) (Katzberg Col. 2:60-64). A renal filtration fraction (FF) is calculated using the measured T_1A and T_1V and also using a baseline (no Gd-DTPA) T_1 value (T_1B) by Equation (5) (Katzberg Col. 3:10-14). The Gd-DTPA paramagnetic contrast agent notably affects the rate of change in image intensity, and the renal FF is estimated using the T_1 values rather than by using the absolute image intensity values (or a difference in image intensity values) in the MRI image. In my opinion, the MRI image intensity values cannot be used to estimate the renal FF directly, as the difference between the artery image and vein image intensity values changes over time as shown by the image intensity plots of the Figure in Katzberg. Specifically, for inversion times less than approximately 380ms and more than 1200ms, the vein image intensity exceeds the artery image intensity, while from 380ms to 1200ms the artery image intensity exceeds the vein image intensity. The difference between the MRI artery image intensity and the MRI vein image intensity of Katzberg provides no meaningful results about the renal FF because Gd-DTPA affects MRI images non-linearly. For an MRI image, the rate of change of the exponential curves matters, not the absolute image intensities. Thus, it is my view that a personal of ordinary skill in the art cannot conclude based on Katzberg that a renal extraction fraction can be measured using MRI image intensities, nor is it obvious from Katzberg to use

CT numbers (CT image intensities) instead of MRI image intensities to assess renal functions as claimed in my patent application.

7. In my opinion, Unger teaches an ultrasound imaging method for diagnosing renal disease using a contrast agent enhanced by an accompanying renal vasodilator (Unger Abstract). While other diagnostic imaging methods are discussed in the Unger patent in general, such as computed tomography (CT), MRI and nuclear magnetic imaging (NMI), Unger primarily teaches measuring image contrast in ultrasound analog video data, referred to as "videodensitometry", with a contrast agent that includes a gaseous component (Unger Col. 10:25-37). A renal vasodilator is also applied to increase blood flow to renal tissue and therefore increase the concentration of contrast agent in renal tissue relative to associated vasculature (Unger Col. 13:29-40). Unger provides no discussion about measuring renal extraction fraction with ultrasound or with any of the other imaging methods briefly described. Unger describes Gd-DTPA as a contrast agent for MRI but does not recommend MRI contrast agents for measuring blood flow due to low sensitivity at normal levels and toxicity at higher levels (Unger Col. 3:66-4:25). Unger does not recommend Gd-DTPA as a radiographic contrast agent for CT imaging, nor does Unger connect Gd-DTPA with CT methods (or with HU levels in image intensity).

8. My patent application claims a CT imaging method to measure renal function based on CT numbers of arterial blood and venous blood using a radiographic contrast agent. In an embodiment, a renal extraction fraction is computed using a difference in arterial and venous CT numbers (corresponding to arterial and venous image intensities). The arterial or venous image intensities can be calculated as mean CT numbers from multiple measurements at different voxel locations in an arterial or venous region using several axial scans (Application ¶ 0011). Unlike the MRI method of Katzberg, which measures a rate of change in image intensity at a particular location and orientation, the claimed method uses a difference

between mean measured image intensities at different locations in an arterial region and mean measured image intensities at different locations in a venous region.

9. Given my experience and knowledge of diagnostic medical imaging, and after considering Katzberg and Unger, it is my opinion that it would not be obvious to one of ordinary skill in the art to combine the teachings of Katzberg and Unger to arrive at the invention disclosed and claimed in the present application. Katzberg teaches using a time series of MRI images to measure the rate of change in image intensities at a particular location and orientation, while the claimed method uses a difference in CT image intensities measured at different locations in multiple axial scans. Unger focuses on enhancing ultrasound measurements with contrast agents that include gaseous components and an accompanying vasodilator, and Unger does not teach using the MRI paramagnetic contrast agent Gd-DTPA with CT.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I further declare that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both (under Section 1001 of Title 18 of the United States Code), and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: January 15, 2010

Signed: ____________________
Graham Sommer